II. REMARKS

Formal Matters

Claims 30-87 are pending after entry of the amendments set forth herein.

Claims 30-56 were examined and were rejected.

Claims 30, 31, 33, 37, 44, 50, and 55 are amended. The amendments to claims 30, 31, 33, 37, 44, 50, and 55 were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 30, 31, 33, 37, 44, 50, and 55 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 8, lines 9-20; page 12, lines 14-19 . Accordingly, no new matter is added by these amendments.

Claims 57-87 are added. Support for new claims 57-87 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claims 57 and 58: page 9, lines 4-17; claims 60 and 61: page 8, lines 9-20; claims 62 and 64: page 6, lines 24-26; claims 65-67: page 20, lines 1-22; claims 69-70: page 10, line 30 to page 11, line 5; claim 71: page 10, lines 19-20; claims 72-74: page 13, lines 14-23; claim 75: page 8, lines 9-20; claim 76: page 6, lines 24-26; claims 77-83: page 20, page 9, lines 13-17, and page 6, lines 24-26. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Obviousness-type double patenting

Claims 30-56 were rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-6 of U.S. Patent No. 6,265,192.

Applicants enclose herewith a terminal disclaimer, disclaiming patent term beyond the expiration date of U.S. Patent No. 6,265,192. Thus, this rejection of claims 30-56 may be withdrawn.

Claims 30-56 were rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 5-10 and 12 of U.S. Patent Application No. 10/007,262, published as U.S. 2002/0164748.

Applicants will submit a Terminal Disclaimer, disclaiming patent term beyond the expiration date of U.S. 2002/0164748 upon issuance of U.S. 2002/0164748 or upon receipt of a Notice of Allowance in the instant case.

Claim objections

The Office Action stated that claims 37-42, 44-50, 55, and 56 were objected to because claims 37-42, 44-50, 55, and 56 recite "glycosylsulfotransferase-3" while other claims recite "glycosyl sulfotransferase-3."

Claims 37, 44, 50, and 55 are amended to recite "glycosyl sulfotransferase-3."

Sequence compliance

The Office Action stated that sequence identifiers were not provided for the sequences disclosed in Figures 2-4 and on page 38.

Applicants respectfully request entry of the amendments to the specification, as noted above, which amendments insert sequence identifiers. Applicants also provide herewith a set of formal drawings, which include sequence identifiers.

Rejection under 35 U.S.C.§112, second paragraph

Claims 31-36 were rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite. Claims 36, 50, and 54 were rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite.

Claims 31-36

The Office Action stated that claim 31 recites the phrase "under stringent conditions," and stated that the metes and bounds of this phrase are not clear. Applicants respectfully traverse the rejection.

Those skilled in the art are aware of what the stringent hybridization conditions are. Such conditions have been known to those of ordinary skill in the art for at least 20 years. Those skilled in the art would recognize the term "hybridizes under stringent condition." Furthermore, the specification states that stringent conditions are, for example, hybridization at 50°C or higher and 0.1 X SSC, which is defined in the specification. Specification, page 12, lines 17-19. Accordingly, the phrase "under stringent conditions" is clear, and claim 31 need not be amended.

Nevertheless, and solely in the interest of expediting prosecution, claim 31 is amended to recite "wherein stringent hybridization conditions comprises hybridization at 50°C or higher in a solution comprising 15 mM sodium chloride and 1.5 mM sodium citrate."

Claims 36, 50, and 54

The Office Action stated that claims 36, 50, and 54 recite the phrase "substantially free of other proteins," and stated that the metes and bounds of this phrase are not clear. Applicants respectfully traverse the rejection.

The specification states that GST-3 proteins are purified, e.g., substantially free of non-GST-3 proteins, e.g., less than 90%, less than 60%, or less than 50% of the composition is made up of non-GST-3 proteins. Specification, page 7, lines 23-30. The specification further states that in some embodiments the GST-3 protein is present as an isolate, e.g., substantially free of both non-GST-3 proteins and other naturally occurring biological molecules, e.g., less than 70%, less than 60%, or less than 50% of the composition is a non-GST-3 naturally occurring biological molecule. Specification, page 7, line 30 to page 8, line 6. Accordingly, the phrase "substantially free of other proteins" is clear, and claims 36, 50 and 54 need not be amended.

Conclusion as to the rejections under 35 U.S.C.§112, second paragraph

Applicants submit that the rejection of the claims discussed above under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejections under 35 U.S.C.§101 and 35 U.S.C.§112, first paragraph

Claims 30, 37-53, 55, and 56 were rejected under 35 U.S.C.§101, as allegedly lacking utility. Claims 30, 37-53, 55, and 56 were rejected under 35 U.S.C.§112, first paragraph, as allegedly not enabled.

Rejection under 35 U.S.C.§101

The Office Action stated that Applicants have asserted only generalized utilities such as research applications, diagnostic applications, therapeutic agent screening/discovery/preparation applications as well as therapeutic compositions. The Office Action stated that the asserted utility of the claimed

polynucleotides and its fragments is not substantial or specific. Applicants respectfully traverse the rejection.

Discussion of Relevant Portions of the Utility Examination Guidelines, Training Materials, and the Law Relating to Same

Utility Examination Guidelines

The Utility Examination Guidelines state that Office personnel are to adhere to the following procedures when applying a rejection under 35 U.S.C. §101. Any rejection based on lack of utility should include a detailed explanation as to why the claimed invention has no specific and substantial credible utility[1]. Whenever possible, the Office should provide documentary evidence[2]. In the absence of documentary evidence, the Office must provide a prima facie showing that establishes that it is more likely than not that a person skilled in the art would not consider credible any specific and substantial utility asserted by the Applicants for the claimed invention. A prima facie showing must contain the following elements: (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; (2) support for factual findings relied upon in reaching this conclusion; and (3) an evaluation of all relevant evidence of record[3]. *A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record.* Utility Examination Guidelines, *Federal Register* (Jan. 5, 2001) Vol. 66(4):1092-1099, emphasis added.

The specification provides a number of specific and substantial utilities for the claimed nucleic acids that would be deemed specific, substantial, and credible by those skilled in the art.

The specification states that the nucleic acids are useful for a variety of applications, including: (1) as probes and primers; Specification, page 12, lines 7-8 and lines 11-23, and page 13, lines 14-23; (2) to identify expression patterns for GST-3; Specification, page 12, lines 8-9, and page 13, line 24 to page 14, line 4; (3) in diagnostic applications, to determine the expression level of GST-3; Specification, page 16, lines17 to 28; and (4) for preparing GST-3 polypeptides; Specification, page 10, lines 27-30.

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[1]Fed. Reg. Vol. 66 at page 1098, Section II-B, paragraph 3.

[2]Fed. Reg. Vol. 66 at page 1098, Section II-B, paragraph 3.

[3]Fed. Reg. Vol. 66, at page 1098, Section II-B, paragraph 3.

GST-3 polypeptides and fragments are in turn useful in e.g., screening assays, to identify agents that modulate GST-3 activity. Specification, page 20, lines 1-3. GST-3 fragments include functional domains such as a sulfate acceptor binding site (Specification, page 8, line 14; and page 38, line 24); and a donor binding site, e.g., VRYEDL (Specification, page 8, line 15).

Thus, the specification provides a number of specific and substantial utilities that those skilled in the art would find credible. Accordingly, instant claims 30, 37-53, 55, and 56 comply with the requirements of 35 U.S.C.§101.

The Office Action stated that Applicants "do not identify even a single specific disease that can be treated using any of the above so called agents or more specifically the polynucleotides claimed in the above claims" and further stated that "there is no information that links the use of the polynucleotide with SEQ ID NO:1 and its fragments to any specific disease state." Office Action, page 4. However, there is no requirement under 35 U.S.C.§101 that a claimed nucleic acid have utility in treating a disease.

Furthermore, the specification discusses the involvement of sulfotransferases in sulfation of selectin ligands, and discusses the fact that selectin mediated binding plays an important and prominent role in biological processes such as leukocyte homing, immune surveillance, and inflammation. Specification, page 2, lines 3-26. The specification discusses the fact that GST-3 is expressed on high endothelial venules (HEV). Specification, page 7, lines 4-10; and page 34. Leukocyte binding to HEV is known to be a critical step in leukocyte homing. The specification identifies a number of disorders involving selectin-mediated binding events, including disease conditions associated with homing of leukocytes to sites of inflammation. Specification, page 30, lines 13 et seq.

Rejection under 35 U.S.C.§112, first paragraph

Claims 30, 37-53, 55, and 56 are supported by a specific an substantial asserted utility. Accordingly, and as discussed in more detail below, those skilled in the art, given the ample description in the specification as noted above, would know how to use the nucleic acids as claimed. Thus, claims 30, 37-53, 55, and 56 also comply with the requirements of 35 U.S.C.§112, first paragraph.

Conclusion

Applicants submit that the rejections of claims 30, 37-53, 55, and 56 under 35 U.S.C. §101 and under 35 U.S.C.§112, first paragraph has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, first paragraph

Claims 30-56 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Claims 30-56 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description.

Enablement

The Office Action stated that the specification does not reasonably provide enablement for any DNA including variants, mutants, and recombinants which are fragments of SEQ ID NO:1 encoding either a fragment of amino acids of SEQ ID NO:2 without any catalytic activity but exhibiting sulfate donor or sulfate acceptor sequences. Applicants respectfully traverse the rejection.

The Office Action stated that Applicants have not provided any credible asserted utility or a well-established utility for the claimed polynucleotides or the polypeptides encoded by the polynucleotides. However, as discussed above, The specification states that the nucleic acids are useful for a variety of applications, including: (1) as probes and primers; Specification, page 12, lines 7-8 and lines 11-23, and page 13, lines 14-23; (2) to identify expression patterns for GST-3; Specification, page 12, lines 8-9, and page 13, line 24 to page 14, line 4; (3) in diagnostic applications, to determine the expression level of GST-3; Specification, page 16, lines17 to 28; and (4) for preparing GST-3 polypeptides; Specification, page 10, lines 27-30. As discussed in the specification, GST-3 polypeptides and fragments are in turn useful in e.g., screening assays, to identify agents that modulate GST-3 activity. Specification, page 20, lines 1-3. GST-3 fragments include functional domains such as a sulfate acceptor binding site (Specification, page 8, line 14; and page 38, line 24); and a donor binding site, e.g., VRYEDL (Specification, page 8, line 15). Thus, the specification provides a number of specific and substantial utilities that those skilled in the art would find credible.

Furthermore, as discussed in detail below, Applicants have provided ample guidance for how to use the nucleic acids as claimed.

The law regarding enablement of inventions is clear: "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."[4]

To aid in determinations of enablement, courts have identified eight factors for consideration: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability or unpredictability of the art; and (h) the breadth of the claims.[5]

The MPEP states that "[i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others." The Office Action considered only one of the factors, and ignored the others. The factors must all be considered in an enablement analysis; no one factor is dispositive.

The instant specification teaches how to make the claimed nucleic acids, and how to use the claimed nucleic acids. The specification discusses various uses for the claimed nucleic acids, including (1) as probes and primers; Specification, page 12, lines 7-8 and lines 11-23, and page 13, lines 14-23; (2) to identify expression patterns for GST-3; Specification, page 12, lines 8-9, and page 13, line 24 to page 14, line 4; (3) in diagnostic applications, to determine the expression level of GST-3; Specification, page 16, lines17 to 28; and (4) for preparing GST-3 polypeptides; Specification, page 10, lines 27-30. Using no more than standard techniques well known to those skilled in the art, and the ample guidance provided in the instant specification, those skilled in the art could readily make a claimed nucleic acid and use same in any of the above-mentioned applications.

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[4] *United States v. Telectronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997); *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

[5] *Ex Parte Forman.*, 230 USPQ 546, 547 (Bd.Pat.App & Interf. 1986); and, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Applicants respectfully submit that the specification, coupled with the information known in the art, would enable one of skill in the art to use the invention without undue experimentation. Relevant enablement factors are discussed in detail below.

(a) the quantity of experimentation necessary:

The courts have clearly taught that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. For example, see MPEP §2164.01.[6]

As the court explained[7]:

"[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."

Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, the court concluded that extensive screening experiments, while being voluminous, were not undue in view of the art which routinely performs such long experiments.[8]

Claim 30 now depends from claim 57, and recites a nucleic acid comprising a fragment of at least about 25 contiguous nucleotides of a nucleotide sequence having at least about 90% nucleotide sequence identity to the nucleotide sequence set forth in SEQ ID NO:01; claim 37 now depends from claim 60 and recites a nucleic cid comprising a sequence that encodes a fragment of at least about 15 contiguous amino acids of the sequence depicted in SEQ ID NO:02, wherein the fragment comprises a sulfate acceptor binding site of GST-3; claim 44 recites a nucleic cid comprising a sequence that encodes a fragment of at least about 15 contiguous amino acids of the sequence depicted in SEQ ID NO:02, wherein the fragment comprises a sulfate acceptor donor site of GST-3; claim 51 recites an isolated nucleic acid comprising at least 25 contiguous nucleotides of the sequence set forth in SEQ ID

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[6] See also *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985).
[7] *In re Wands* 8 USPQ 2d at 1404
[8] *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

NO:01; claim 55 recites an isolated nucleic acid comprising a sequence that encodes a fragment of at least about 15 contiguous amino acids of a polypeptide having at least about 60% amino acid sequence identity to the sequence depicted in SEQ ID NO:02, wherein the fragment comprises a sulfate acceptor binding site of GST-3; and claim 56 recites an isolated nucleic acid comprising a sequence that encodes a fragment of at least about 15 contiguous amino acids of a polypeptide having at least about 60% amino acid sequence identity to the sequence depicted in SEQ ID NO:02, wherein the fragment comprises a sulfate donor binding site of GST-3.

The only experiments, if any, that need be performed to enable the entire scope of the claim are those designed to determine whether a given fragment catalyzes transfer of a sulfate group from a sulfate donor to a sulfate acceptor, comprises a GST-3 sulfate acceptor binding site, or comprises a GST-3 sulfate donor binding site. Adequate guidance is given in the specification, and relevant information was known to those skilled in the art. Any experimentation, if necessary, would involve routine techniques well known to those skilled in the art.

The sequence of polypeptides retaining sulfate acceptor binding or sulfate donor binding activity is determined through routine experimentation, typically employing nothing more than performing the same assay disclosed in the specification on a variety of sequence variants of the polypeptide made by routine recombinant DNA techniques. Since these experiments are routine in nature, no undue experimentation is required. In other words, the only experimentation that may be required to enable the claimed invention are those experiments to determine the presence of a certain activity, and since this only requires a routine assay on polypeptide variants to determine the active fragments and/or active variants, no undue experimentation is necessary.

(b) the amount of direction or guidance presented

As discussed above, the specification provides ample guidance for making and using nucleic acids as claimed. For example, the specification states that nucleic acid fragments are prepared by chemically synthesizing oligonucleotides in accordance with conventional methods, by restriction enzyme digestion, by polymerase chain reaction amplification, etc. Specification, page 10, lines 17-20. The specification provides guidance for use of a claimed nucleic acid as a probe or a primer

(Specification, page 12, lines 7-8 and lines 11-23, and page 13, lines 14-23); in identifying expression patterns for GST-3 (Specification, page 12, lines 8-9, and page 13, line 24 to page 14, line 4); in diagnostic applications, e.g., to determine the expression level of GST-3 (Specification, page 16, lines17 to 28); and in the preparation of GST-3 polypeptides (Specification, page 10, line 27 to page 11, line 27).

(c) the presence or absence of working examples:

Compliance with the enablement requirement under Section 35 U.S.C. §112, first paragraph does not require or mandate that a specific example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.[9] Furthermore, "Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples."[10]

Although there is no requirement for working examples, the specification provides working examples of the use of nucleic acid fragments in detecting expression of GST-3. Specification, page 36, line 20 to page 37, line 10. The specification provides also working examples of amino acid sequences encoded by nucleic acids encoding sulfate acceptor binding sites. Specification, page 38, line 24.

(f) the relative skill of those in the art:

The relevant ordinarily skilled artisan is generally a skilled laboratory technician with experience in molecular biology and/or a scientist with the equivalent of a doctoral degree in molecular biology techniques. Furthermore, such artisans are required to keep abreast of the latest technology through continuing education and reading of scientific journal articles. As such, the skill level of those developing and using methods for generating a nucleic acid and generating polypeptides encoded by the nucleic acid is high.

(g) the predictability or unpredictability of the art

The Office Action stated that Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of

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[9] In re Borkowski, 164 USPQ at 645.

the claims, and that without sufficient guidance, determination of the use of the claimed DNAs is unpredictable.

However, as discussed above, the level of skill in the art is very high with respect to generating nucleic acid fragments, with respect to producing polypeptides encoded by a given nucleic acid, and to determining the activity of a given polypeptide.

Furthermore, the courts have clearly taught that even in unpredictable arts the specification does not have to disclose every species of a genus that would work and every species that would not work.

The court has very clearly explained: [11]

> To require such a complete disclosure would apparently necessitate a patent application or applications with thousands of catalysts....More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid literal infringement of such claims by merely finding another analogous catalyst complex which could be used ....

Because every species in a genus does not have to be tested for a genus to be enabled, extensive disclosure or guidance of the active species of a genus does not have to be provided for a genus of this scope to be enabled.

(h) the breadth of the claims

Those skilled in the art could readily prepare and use nucleic acids commensurate in scope with the claims.

The specification therefore provides sufficient enablement such that one of ordinary skill in the art would be able to practice the invention without undue experimentation.

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[10] *In re Robins* 166 USPQ 552 at 555 (CCPA 1970).

Written description

The Office Action stated that the specification does not contain any disclosure of the function of all DNA sequences encompassed by the claims or the amino acid sequences encoded by the DNA sequences. Applicants respectfully traverse the rejection.

Consideration of the standards for written description

The Revised Interim Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, paragraph 1 "Written Description" Requirement, (*Federal Register* (Dec. 21, 1999) Vol. 64 (No. 244):71427-71440) ("Revised Guidelines"), state:

(1) There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed;

(2) the Office has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims;

(3) Consequently, rejection of an original claim for lack of written description should be rare;

(4) an Examiner should review the entire application to understand what the applicant has described as the essential features of the invention; and

(5) the Examiner's review of the application is to be conducted *from a standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art* (emphasis added). Revised Guidelines, at page 71435.

The Office Action has not presented sufficient evidence or reasons why a person skilled in the art would not recognize that the written description of the claimed invention provides support for the claims.

As stated in the Revised Guidelines, "In most technologies which are mature, and *wherein the knowledge and level of skill in the art is high*, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention." Revised Guidelines, page 71436. The written description guidelines are based in part on *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir.1997). It should be remembered that *University of California v. Eli Lilly and Co.*, (Fed. Cir.1997) was based on a

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[11] *In re Angstadt*, 190 USPQ at 218.

patent that was filed in 1977, i.e., over 20 years ago, when the level of skill in the art was not at the level that it was as of the filing date of the instant application.

The purpose of the written description requirement is to ensure that the specification conveys to those skilled in the art that the applicants possessed the claimed subject matter as of the filing date sought. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). *See also All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 2002 U.S. App. LEXIS 22372, *10-11 (Fed. Cir. October 25, 2002) (the specification must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed."). Thus, the test for whether a claimed invention is adequately described has often been stated as whether or not one of skill in the art would have understood from the specification that an applicant possessed the claimed subject matter when the specification was filed. *See, e.g., Ralston Purina Co. v. Far-Mar-Co, Inc.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. (BNA) 177, 179 (Fed. Cir. 1985). Whether the specification meets the written description requirement for the claimed invention is a question of fact. *Vas-Cath,* 935 F.2d at 1563, 19 U.S.P.Q.2d (BNA) at 1116.

The written description requirement of 35 U.S.C.§112, first paragraph, does not require that Applicants disclose the function of all DNA sequences encompassed by the claims or the amino acid sequences encoded by the DNA sequences.

The specification provides the sequence of SEQ ID NO:01. Thus, the specification provides adequate written description of nucleic acids comprising a fragment of at least about 25 contiguous nucleotides of a nucleotide sequence having at least about 90% nucleic acid sequence identity to SEQ ID NO:01. Those skilled in the art, given the description in the specification, would reasonably conclude that Applicants had, as of the priority date of the instant application, possession of the claimed invention. Accordingly, the instant specification provides adequate written description for the claimed invention.

Conclusion as to the rejections under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of claims 30-56 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§103

Claims 45-50 were rejected under 35 U.S.C.§103 as allegedly unpatentable over Aparicio et al. (PIR Database, Accession No. T30228 and *Gene* 169:9-16; "Aparicio") in view of Sambrook et al. (Molecular Cloning, A Laboratory Manual, 2nd ed. Cold Spring Harbor Press, 1989; "Sambrook").

The Office Action stated: (1) Aparicio teaches a polypeptide comprising the peptide VRYEDL; (2) Aparicio does not teach a nucleic acid encoding the peptide; and (3) Sambrook teaches in general recombinant methods for converting a peptide sequence into a DNA sequence. The Office Action concluded that it would have been obvious to one of ordinary skill in the art interested in making the peptide fragment by a recombinant method as opposed to a synthetic method. Applicants respectfully traverse the rejection.

There is no disclosure or suggestion in Aparicio of a nucleic acid that encodes a sulfate donor binding site, as required by claim 45. Aparicio discusses domains of polypeptides of rapamycin-producing polyketide synthase. Aparicio states that the domains are acyl-carrier protein, β-ketoacyl-ACP synthase, acyltransferase, enoyl reductase, β-ketoacyl-ACP reductase, dehydratase, and coenzyme 1 ligase. Aparicio, Summary. Aparicio neither discloses nor suggests a sulfate donor binding site. Accordingly, Aparicio cannot render instant claims 45-50 obvious.

Sambrook does not cure the deficiency of Aparicio. Without any guidance in Aparicio to select a fragment that comprises a sulfate donor binding site, one of ordinary skill in the art interested in making a fragment comprising a sulfate donor binding site by a recombinant method would not know which fragment of the sequences discussed in Aparicio to select.

The Office Action stated that Aparicio provides motivation because "Aparicio et al. teach that said peptide is a fragment of a carrier protein and using such fragment one of ordinary skill in the art can raise specific antibodies for the same." Office Action, page 9. However, Aparicio does not specifically mention any sulfate donor binding site, much less a sulfate donor binding site comprising VRYEDL. Indeed, PIR Database, Accession No. T30228 indicates that the sequence VRYEDL resides in residues 4365-4370, which is not part of any of the domains mentioned in Aparicio. Thus, there would be no motivation for a person skilled in the art to select the sequence VRYEDL from the sequence discussed

in Aparicio.

There is no motivation for one of ordinary skill in the art to combine the cited references. Even if the cited references were combined, one would not arrive at the present invention. Accordingly, Aparicio, alone or in combination with Sambrook, cannot render instant claims 45-50 obvious.

Applicants submit that the rejection of claims 45-50 under 35 U.S.C. §103 has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL107CON.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: July 29, 2003

By: _____
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